UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,768	05/04/2005	Piero Chiarelli	0002263USU/3061	8171

27623 7590 12/04/2009

OHLANDT, GREELEY, RUGGIERO & PERLE, LLP
ONE LANDMARK SQUARE, 10TH FLOOR
STAMFORD, CT 06901

EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,768	CHIARELLI ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34 - 36, 38 - 50* is/are pending in the application.

4a) Of the above claim(s) *46 - 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34 - 36, 38 - 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed September 10, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Election/Restrictions

1. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 34 – 36, 38 – 42 and 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios (US 2002/0004065). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 6, 209 and those set forth below.

Applicant traverses this rejection on the grounds that as acknowledged in the Office Action, "Kanios does not explicitly prepare a composition with rifaximin and PVA" (polyvinyl alcohol) and thus fails to disclose two technical features of the claimed invention. Kanios relates to transdermal drug delivery systems providing substantially zero order release profiles for an extended period of time of up to 7 days or longer. Kanios also does not pertain to the same field of endeavor as the current claims. Kanios discloses a practically unlimited list of possible active agents to be delivered. At ¶ [0046] where Kanios discloses the crystallization inhibitor, another practically unlimited list of possible substances is given but in subsequent paragraphs and the examples, only

PVP (polyvinyl pyrrolidone) is actually further described for use as the crystallization inhibitor. A person having ordinary skill in the art at the time of the instant invention would not have considered Kanios as Kanios pertains to a different field of endeavor, but even if such a person were to have considered Kanios, that person would never have been aware of the specific and peculiar problem involved with the use of rifaximin. The current disclosure describes devices that make possible the use of rifaximin outside the intestine that in particular allow high-level, constant in time, of concentration of rifaximin in aqueous body fluids avoiding the intense red color that it produces in the area surrounding the administration site. The person of ordinary skill in the art would have never taken into consideration Kanios, teaching how to eliminate or suppress the higher initial release of drug for solving the problem of administering high levels, constant in time of concentration of rifaximin in aqueous body fluids that avoids the intense red color that it produces in neighboring areas. The highlights even more the criticality of the claimed combination. The conclusion of the Office Action requires impermissible hindsight.

These arguments are unpersuasive. Merely because a reference does not explicitly teach the claimed combination of polyvinyl alcohol and rifaximin (which the Examiner assumes to be the two technical features that Applicants assert are not disclosed), the reference taken as a whole renders obvious the claimed combination. The teachings of a reference are not limited to the examples but are prior art for all that they disclose.

The drug delivery system of Kanios is taught as generally applicable to a wide variety of drugs and among the active agents listed is rifaximin. When one of ordinary skill wished to prepare a formulation of rifaximin, due to the disclosure of Kanios, such a person would be taught that the disclosed drug delivery system of Kanios is suitable for the delivery of rifaximin. Below is paragraph [0045] wherein the various crystallization inhibitors are disclosed by Kanios:

> [0046] A crystallization inhibitor or solubility enhancer may also be employed in the invention, for example polyvinylpyrrolidone polymers, polyethylene oxide, polyacrylic acid, polyvinyl alcohol, silicone dioxide, silica, celluloses and cellulose derivatives such as hydroxymethyl cellulose, hydroxypropyl cellulose, gelatins, gums, starches, dextrins and dextrans, sterols, bile acids and other absorptive agents that possess the capability to absorb and hold water or moisture.

While the list concludes with the "other absorptive agents that possess the capability to absorb and hold water" which does encompass more compounds than those explicitly listed, polyvinyl alcohol is one of the compounds that is explicitly taught to as functionally equivalent to the polyvinyl pyrrolidone.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., high-level, constant in time, of concentration of rifaximin in aqueous body fluids avoiding the intense red color that it produces in the area surrounding the administration site) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The release profile from the devices of Kanios are zero-order, which means that the release rate is

independent of the amount of the drug remaining in the device, which is a "constant in time" release. Additionally, in response to applicant's argument that the device as recited avoids a red coloration from developing in the area surrounding the administration, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicants never indicate what the field of endeavor for either the instant claims or Kanios is. The instant claims are drawn to a device for controlled delivery of rifaximin. Kanios is drawn to a device, more specifically a transdermal device, for the controlled delivery of active agents such as rifaximin that has the same elements as recited in the instant claims. Therefore, both the instant claims and Kanios are drawn to controlled release drug delivery devices and are in the same field of endeavor.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As discussed above, the selection of the active ingredient and polyvinyl alcohol as the crystallization inhibitor based on the disclosure of Kanios takes into account only

knowledge which was within the level of ordinary skill at the time the claimed invention was made so no improper hindsight reasoning was employed.

6. Claims 34 – 36 and 38 – 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios and further in view of Govil et al. (US 4,908,213). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 6, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that there would not have been any reason why a person having ordinary skill in the art would combined Kanios, regarding a system designed to eliminate or suppress the higher initial release of drugs with Govil, regarding a patch comprising nicotine and at least one antipruritic compound in order to address or and solve the specific problem of rifaximin. Even if such a person had combined the two references that person would have been led, at most to believe that when nicotine is used as an active agent, the transdermal delivery system of Kanios must include at least one antipruritic compound,

These arguments are unpersuasive. Govil was cited for its teachings regarding the physical structure of the adhesive, comprised of acrylic polymers, optionally containing active substance, that can be applied to the surface of polymeric materials such as PVA and PVP (see p 7, ¶ 4 of April 6, 2009 Office Action). Applicants have not presented any arguments as to why one of ordinary skill would not, in light of Kanios and Govil that both relate to transdermal drug delivery system, would not be taught that the bio-adhesive polymer (the acrylic polymer) could not be either homogenously mixed

into the polymeric matrix (such as polyacrylates) as required in claim 42 and taught by both Kanios and Govil or applied to the surface of the polymeric matrix as taught by Govil. Therefore, this rejection is maintained.

7. Claims 34 – 36, 38 – 42, 44 and 45 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios further in view of Wharton (US 6,194,455).

Applicant traverses this rejection on the grounds that Wharton clearly does not relate to the same field of endeavor as its sole claim is directed towards a method of preventing a nascent herpes outbreak from developing into a herpes ulcer by topical administration of sucralfate and lidocaine in a particular ratio with an antibiotic and pharmaceutically acceptable carrier to a site identified as nascent herpes outbreak. Kanios has already disclosed the possibility of one or more active agents and a practically unlimited list of substances ac active substances. Thus, the person having ordinary skill in the art would not have found disclosed in Wharton any additional information with respect to what had already been disclosed by Kanios.

These arguments are unpersuasive. Once again, Applicant does not state the field of endeavor for the two pieces of art that have been applied. While the claim of Wharton is a method, that method utilizes a topical composition for the delivery of active ingredient. Kanios does not explicitly identify a combination of rifaximin, an antibiotic, with another antibiotic and/or an anti-inflammatory and/or pain reliever and/or anesthetic drug. While Kanios may disclose that more than one active ingredient can be present, Wharton was cited to show that the specific combination of an antibiotic with another

antibiotic and/or an anti-inflammatory and/or pain reliever and/or anesthetic drug was known in the art and set forth reasons as to why such a combination (prevent infection and relieve pain, 8 - 9 of April 6, 2009 Office Action) would be selected from the possible combinations that exist for the active ingredients presented in Kanios. Therefore, this rejection is maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW